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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,685	07/18/2005	Larry I. Benowitz	701039-52287	4644

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EXAMINER	
KRISHNAN, GANAPATHY	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
12/15/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/528,685	BENOWITZ, LARRY I.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/11/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 10/27/2008 has been entered.

The Request for Continued Examination filed 10/27/2008 has been carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1-33 have been canceled.

2. New Claims 34-38 have been added.

3. Remarks drawn to rejections maintained in the previous action.

Claims 34-38 are pending in the case.

Information Disclosure Statement

Foreign language references listed in the Information Disclosure Statement, for which no English translation has been provided, have not been considered. If an English abstract has been provided or available for a foreign language document then only the English abstract has been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the regeneration of axons on retinal ganglion cells by administration of mannose and forskolin, does not reasonably provide enablement for the regeneration of neurons using a combination of D-mannose and all the modulators as broadly claimed in instant claims 35-36. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art
(C) The level of predictability in the art
(D) The amount of direction provided by the inventor
(E) The existence of working examples
(F) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claims 35-36 are drawn to a method of promoting neuron outgrowth by administering a therapeutically effective amount of D-mannose in combination with cAMP modulators. The breadth of the claims is seen to include several such modulators including ones that are not known at the time of filing of the instant application.

The state of the prior art

The examiner notes that the art cited by the applicants and the prior art of record, Thanos et al (Investigative ophthalmology and Visual Science, 2000, 41(12), 3943-54) is drawn to axonal regeneration promoted by some growth factors. However, there is no teaching of axonal regeneration using any other modulator in the prior art. One of ordinary skill in the art would not extrapolate the information in the prior art to the instant method using all modulators as instantly claimed.

The level of predictability in the art

Based on the teaching of the prior art it is highly unpredictable that any modulator will promote the growth of neurons in combination with D-mannose.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the outgrowth of neurons as instantly claimed. Even though the specification (page 1) mentions references

The existence of working examples

The working examples set forth in the instant specification are drawn to the effect of mannose and mannose forskolin combination on rat ganglion cells. The results show axons regeneration. Despite these examples there is little enabling disclosure for the generation of axons using any cAMP modulator. Forskolin is not representative of all cAMP modulators as instantly claimed. Applicant is therefore not entitled to claim all of the modulators as recited in instant claims 35-36.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the use of the modulators in combination with D-mannose in the method as instantly claimed. One of ordinary skill in the art would have to carry out experimentation with several different modulators to determine the efficacy of the said compounds in the said methods of treatment.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd.

App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 36 recites the broad recitation phosphodiesterase inhibitors, and the claim also recites specific phosphodiesterase IV inhibitors which is the narrower statement of the range/limitation.

Claim 36 recites the term analogue. In the absence of the specific chemical names of the analogues of this invention, the identity of said analogues would be difficult to define and the metes and bounds of the said analogues applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claim.

Claims 37-38 are drawn to the method further comprising oncomodulin and TGF-β, respectively. According to the applicant's (specification, page 9) oncomodulin and TGF-β are macrophage derived factors. Does applicant intend a method further comprising another cAMP modulator other than oncomodulin and TGF-β. The claim language is not clear.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d

2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 34-38 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 6-9 of copending Application No. 10/580,364 ('364). Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant Claim 34 is drawn to a method of promoting neuronal outgrowth in a neuron comprising administration of an effective amount of D-mannose (a hexose). Dependent claims recite limitations drawn to the type of hexose and other active agents.

Claims 1-4 and 6-9 of '364 differ from the instant claims in that the instant claims do not employ an NgR antagonist. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the active agents as recited in the instant claims could be successfully employed in the method of '364 too since both are used to promote the growth of neurons.

In determining the differences between the prior art and the claims, the question is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found

either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). In the instant case, '364 teaches the use of some of the active agents applicant claims. Although the claims of '364 employ an NgR antagonist in combination with the active agents instantly claimed, one of ordinary skill in the art would readily recognize that the scheme taught by '364 could be employed in the instant method. The use of known members of classes of agents in a method to effectuate the same type of treatment taught in the prior art is not seen to render the instantly claimed method unobvious over the art. Once the general method of using the active agents has been shown to be old, the burden is on the applicant to present reason or authority for believing that the starting compound (s) would alter the nature of the product or the operability of the method and thus the unobviousness of the method of treatment.

Conclusion

Claims 34-38 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/

Examiner, Art Unit 1623

/Shaojia Anna Jiang/

Supervisory Patent Examiner, Art Unit 1623